

## **REMARKS**

### **Preliminary Remarks**

Reconsideration and allowance of the present application based upon the foregoing amendment and following remarks are respectfully requested. Claims 17-20, 22-30, 32, and 33 are currently pending. Claims 17-19, 22, 23 and 33 have been allowed. Claims 24-30 and 32 remain at issue.

In paragraph 5 of the official action, the examiner objected to claim 20 under 37 C.F.R. §1.75(c) as being in improper dependent form for failing to further limit the subject matter of a previous claim. Although the applicants believe claim 20 is distinguishable over claims 17 and 19 due to it being directed to “degenerative variants thereof,” the applicants have canceled claim 20 without prejudice in order to expedite prosecution.

New claims 34-39 are directed to vectors and host cells expressing the variant sequences of claims 25 and 26. Support for new claims 34-39 can be found throughout the specification, for example, on page 12, line 12 to page 13, line 19 and page 18, lines 20-25.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

### **Patentability Remarks**

#### ***Rejection Under 35 U.S.C. §112, First Paragraph***

In paragraph 6 of the official action, the examiner rejected claims 24-30 and 32 under 35 U.S.C. §112, first paragraph, for lack of enablement. Specifically, the examiner alleged that while the specification is enabled for polynucleotides encoding SEQ ID NO: 2, the specification does not reasonably provide enablement for polynucleotides encoding amino acids sequences that are at least 80%, 90%, or 95% identical to SEQ ID NO: 2. The examiner further asserts the positions within the encoding nucleic acid's sequence where modifications are highly unpredictable and cannot be made with a reasonable expectation of success in obtaining an encoded polypeptide having the desired activity. The examiner further alleged that while methods of generating variants of a given polynucleotide (*e.g.*, mutagenesis), and methods of isolating homologous polynucleotides (*e.g.*, hybridization) are

known, it is not routine in the art to screen for all polynucleotides having a substantial number of substitutions or modifications as encompassed by the instant claims. The examiner concluded the applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims without undue experimentation.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claim 24 without prejudice, thereby obviating the rejection of this claim. Dependent claims 27-30, 32, and 33 have been amended to be ultimately dependent upon allowed claims 17-19, 22 and 23, thereby rendering the rejection to these claims moot.

The issue of enablement involves the question of whether an application enables one of ordinary skill in the art to make and use the claimed invention. Experimentation is limited in independent claims 25 and 26 to an isolated DNA encoding a protein containing an amino acid sequence which is at least 90% or 95% identical to the amino acid sequence of SEQ ID NO: 2, and exhibits transaldolase enzymatic activity (see pg. 5, line 25 to pg. 6, line 2). Therefore, there is no question that the variants encompassed by the claims must retain the utility of the DNA sequence discovered and claimed by the applicants, and subsequently, allowed to the applicants. The applicants further submit the specification enables one of skill in the art to make and functionally define the claimed variants, and methods of generating variant polynucleotides are known in the art as acknowledged by the examiner on page 6 of the official action (see also pg. 1, line 22 to pg. 2, line 8).

Specifically, claims 25 and 26 satisfy the "how to make" prong of the enablement requirement because the scope of the claims are "reasonably correlated" with the teachings in the application [See MPEP §2164.01(b)]. The application and ordinary skill permit one skilled in the art to make any polynucleotides having 90% or greater sequence identity to the amino acid sequence recited in the claims by using PCR technology or other mutagenesis techniques discussed on page 1, lines 22-24; page 5, line 25 to page 6, line 2; page 10, line 27 to page 11, line 10. In fact, the Patent Office's own written description training materials acknowledge that "procedure[s] for making variants of [a protein having] SEQ ID NO: [3] which have 95% identity to SEQ ID NO: [3] and retain its enzymatic activity are conventional in the art." (See Revised Interim Written Description Guidelines Training Materials, Example 14). Moreover, the application provides guidance as to the types of

changes (e.g., conservative mutations) that are more likely to retain functionality (see specification, pg. 10, lines 6-20).

The variants recited in claims 25 and 26 are also functionally defined in that the claimed variants are limited to those with transaldolase enzymatic activity (i.e., catalyzing the transfer of a dihydroxyacetone group from sedoheptulose-7-phosphate to glyceraldehyde-3-phosphate resulting in erythrose-4-phosphate and fructose-6 phosphate). The specification specifically refers to the inventors successfully isolating the novel tal gene coding for the enzyme transaldolase from *C. glutamicum* (Example 2). The specification also specifically describes the desired variant polypeptides with at least 90 or 95% identity to the amino acid sequence according to SEQ ID NO: 2 must have transaldolase activity (pg. 5, line 25 to pg. 6, line 2).

Transaldolase activity is a routine screening assay that identified those encoded polypeptides with the activity (D-sedoheptulose-7-phosphatate:D-glyceraldehyde-3-phosphate dihydroxyacetone transferase activity) recited in the claims (See Exhibit A--Sprenger *et al.*, *J. of Bacteriology* 177:5930-5936 (1995); and Follstad *et al.*, *Eur. J. Biochem.* 252:360-371 (1998)). Since the transaldolase assay is routine in the art, one of skill could perform this assay without undue experimentation on 90% or higher variants of the amino acid sequence set forth in SEQ ID NO: 2. For example, the transaldolase assay is performed by measuring for the formation of fructose-6 phosphate from glyceraldehyde-3-phosphate and a donor was monitored by measuring the increase in NADPH concentration in the presence of phosphoglucose isomerase and glucose-6 phosphate dehydrogenase. A spectrophotometer is used to detect the changes in UV absorption in the assay (Sprenger *et al.*, at page 5931 and 5933).

New claims 34-39 are directed to vectors and host cells expressing the variant sequences of claims 25 and 26 and are therefore also fully enabled by the specification. Accordingly, in view of the structural and functional information about the claimed polynucleotides that is provided in the instant application along with knowledge in the art of transaldolase assays that are well known to one of ordinary skill in the art, the applicants submit that claims 25 and 26 and their dependents are supported by an enabling disclosure.

In light of the foregoing amendments and remarks, the applicants submit that the rejection of claims 25 and 26 under 35 U.S.C. §112, first paragraph, for lack of enablement,


has been overcome and should be withdrawn, and a rejection of new claims 34-39 on the same grounds would be improper.

### CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

All objections and rejections having been addressed, it is respectfully submitted that the present application is in a condition for allowance and a Notice to that effect is earnestly solicited.

Respectfully submitted,  
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